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MAPPING OF FUNCTIONAL ACTIVITY IN BRAIN WITH 18F-FLUORO-DEOXYGLUCOSE(+)

Alavi A.(*), Reivich M.(*), Greenberg J.(*) and Wolf A.(**)

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A large body of evidence links the functional activity of a region of the brain to its metabolic function (1). Therefore, by measuring the regional metabolic rate in response to a given stimulus, it should be possible to map the area(s) of the brain activated by that stimulus. The classical technique for the determination of cerebral metabolism (the Kety-Schmidt technique) only provides a measure of average cerebral metabolic rate for the whole brain and therefore provides a measure of global cerebral function (2). For example, it has been shown that in patients with organic dementia, total cerebral blood flow and metabolism are reduced to a degree that correlates well with degree of dementia (3,4). Also, it has been shown that in coma secondary to various underlying disorders, cerebral oxygen consumption is decreased (5). Similarly, with the administration of anesthetic agents, cerebral oxygen metabolism decreases (6). On the other hand, during a seizure, oxygen and glucose consumption rise and subsequently decline during the postictal period (7).

Using intracarotid administration of xenon-133 and a multicrystal scintillation camera, it has been possible to measure regional cerebral blood flow in response to a variety of sensory stimuli (8). Increases in regional cerebral blood flow have been demonstrated in response to somatosensory, visual, and auditory stimuli.

With the introduction of the ^{14}C-2-deoxyglucose (^{14}C-DG) technique, for the first time it became possible to measure the rates of glucose metabolism in specific discrete regions of the brain in different states of functional activity (9). This substrate

(*) University of Pennsylvania School of Medicine, Philadelphia, PA, and (**) Brookhaven National Laboratory, Upton, NY, U.S.A.

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is phosphorylated by hexokinase to ^{14}C-DG-6 phosphate. Because ^{14}C-DG-6-PO_4 is not a substrate for either phosphohexose isomerase or glucose-6-phosphate dehydrogenase, it is essentially trapped in the tissue over the time course of the measurement. A model has been designed based on the assumptions of a steady state for glucose consumption, a first-order equilibration of the free ^{14}C-DG pool in the tissue with the plasma level, and relative rates of phosphorylation of ^{14}C-DG and glucose determined by their kinetic constants for hexokinase reaction. Using an operational equation based on this model, the metabolic rates of glucose are calculated in various regions of brain (utilizing brain slices and autoradiography). ^{14}C is a beta emitter and therefore not suitable for noninvasive imaging in man.

With the synthesis of ^{18}F-2-deoxy-2-fluoro-D-glucose (^{18}F-DG) all of the requirements for a suitable radiopharmaceutical for the determination of local cerebral metabolism have been met. This agent behaves very similarly to ^{14}C-DG and therefore, using the above described model and emission tomography, it has become possible to measure regional cerebral metabolism for the first time in man (10,11).

METHODS AND MATERIALS

Following insertion of a radial artery catheter under local anesthesia, the subjects were made comfortable in the scanner, and the head was positioned securely in a restraining device. The head was extended or flexed to make the orbital-meatal line perpendicular to the horizontal plane. Each subject received 70-140 μCi/kg of ^{18}F-DG intravenously as a bolus. Blood samples were drawn from the radial artery to monitor the time course of the ^{18}F-DG and glucose. Blood was drawn every 15 sec for the first minute, every minute until 10 min, every 5 min until 30 min, and every 15 min until the end of the study. This tissue activity of ^{18}F-DG was measured using the PETT III or V tomographic scanner at the Brookhaven National Laboratory and the Hospital of the University of Pennsylvania respectively (13,14). In each subject multiple tomographic scans were obtained. We measured local cerebral metabolic rates for glucose in a series of volunteers

subjected to a variety of specific sensory stimuli.

The tactile stimulus consisted of rapid but light stroking (2 to 3 Hz) of the volar and dorsal surface of the fingers and hand of one arm (left, N = 2; right, N = 3) with a hand-held brush, which was just stiff enough to cause an appreciable stimulus without causing any discomfort. Subjects were blindfolded to eliminate visual input and wore earplugs to minimize auditory input.

In the visual study, either the left (N = 4) or right (N = 6) visual hemifield was stimulated so as to ensure only hemifield stimulation. The stimulus consisted of a well-illuminated, slowly moving, high-contrast black-and-white pattern of small lines at various orientations as well as abstract color images presented into one visual hemifield. The subjects wore earplugs.

The auditory system was studied in subjects with normal hearing who listened to a tape-recorded factual story presented through earphones to only one ear (left ear, N = 3; right ear, N = 3). Attentiveness to the story was assessed by testing the subject's recall. These subjects were also blindfolded. Six subjects that were blindfolded and wore earplugs acted as controls for all the studies.

RESULTS

The somatosensory input caused the postcentral gyrus contralateral to the stimulus to become metabolically more active (mean ± standard deviation, 9 ± 10.2 percent) than the homologous area in the ipsilateral cortex. This was not significantly different from the controls (1 ± 6.8 percent, $t(9) = 1.5$, $P < .1$). The nonsignificance is due to the large variance in the control subjects at the level of the postcentral gyrus.

The visual stimulus caused the visual cortex contralteral to the stimulated hemifield to become 8 ± 3.0 percent more active than the ipsilateral visual cortex. The asymmetry is significant in comparison with the controls ($t(14) = 4.06$, $P < .01$) who showed a left-right asymmetry of only 0.5 ± 3.0 percent..

The monaurally presented auditory stimulation elevated the metabolic rate in the temporal cortex contralateral to the stimulated ear. This cortex had a metabolic rate of 7 ± 2.5 percent higher than the ipsilateral temporal cortex. This asymmetry is significant in comparison with the controls ($t(8) = 6.02$, $P < .001$), who showed a left right asymmetry of only 1 ± 2 percent.

These studies represent the first measurement of functional activity in vivo in awake man on a regional basis. They demonstrate that the ^{18}F-DG technique is capable of providing functional maps in response to sensory stimulation. With the use of tomographic scanners with higher spatial resolution and sensitivity, along with newer radiopharmaceuticals, it will be possible to obtain much more extensive information about neural activation with a variety of stimuli. This will provide invaluable knowledge in the evaluation of the diseased brain.

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